image

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.: 09/684,725
In Re Application of Lee Harland
Filed: October 6, 2000
Group Art Unit: 1646
Examiner: Li, Ruixiang
Docket No.: PCS10361ADAM
Customer No.: 28523

Box AF
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Enclosed herewith for the Examiner's consideration is a replacement priority document for the above-referenced case. The enclosed priority document contains Figures 1-3, as described in the specification on page 7, lines 1-8.

Respectfully submitted,

Date: March 8th, 2004

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Attachment: Priority document UK 9923888.3

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Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

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Signed A M Brewer.

Dated 5 October 2000

For official use

8 OCT 1999

Your reference
PCS10361PME-PROV

0 8 OCT 1999

9923888.3

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Form 1/77

Patents Act 1977

1 Title of invention

1 Please give the title of the invention

NOVEL POLYPEPTIDE

2 Applicant's details

☐ **First or only applicant**

2a If you are applying as a corporate body please give:

Corporate name
PFIZER LIMITED

Country *(and State of incorporation, if appropriate)*
UNITED KINGDOM

2b If you are applying as an individual or one of a partnership please give in full:

Surname

Forenames

2c **In all cases,** please give the following details:

Address
RAMSGATE ROAD
SANDWICH
KENT

UK postcode CT13 9NJ
(if applicable)

Country UNITED KINGDOM

ADP number *(if known)* 689267 3001

2d, 2e and 2f:
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Second applicant (if any)

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3
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3a Have you appointed an agent to deal with your application?

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⬇ ***Please give details below***

Agent's name
P. M. ENGLAND
Agent's address
PFIZER LIMITED
RAMSGATE ROAD
SANDWICH
KENT
Postcode CT13 9NJ

Agent's ADP number 7758162001

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5 Claiming an earlier application date

5 Are you claiming that this application be treated as having been filed on the date of filing of an earlier application?

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7

The answer must be 'No' if:
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Please supply duplicates of claim(s), abstract, description and drawing(s).

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8 Checklist

8a Please fill in the number of sheets for each of the following types of document contained in this application.

Continuation sheets for this Patents Form 1/77			
Claim(s)	5	Description	11
Abstract	1	Drawing(s)	2+2

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Priority documents *(please state how many)*	
Translation(s) of Priority documents *(please state how many)*	
Patents Form 7/77 - Statement of Inventorship and Right to Grant *(please state how many)*	
Patents Form 9/77 - Preliminary Examination/Search	
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PCS 10361

NOVEL POLYPEPTIDE

Technical field

The present invention relates to a novel polynucleotide sequence which encodes a novel polypeptide belonging to the class of proteins known as G-protein coupled receptors (GPCRs). The present invention also relates, *inter alia*, to processes for producing the polypeptide and its uses.

Background of the invention

Cells and tissues respond to a wide variety of extracellular signalling molecules through the interaction of these molecules with specific cell-surface receptors. One such class of receptors are known as G-protein coupled receptors (GPCRs) and these are characterised by containing a series of 7 hydrophobic transmembrane segments. Upon binding an extracellular ligand to its receptor, intracellular signals are initiated via interactions with heterotrimeric G proteins which in turn can lead to a number of different intracellular events depending upon which receptor has been activated. For example some GPCRs influence adenyl cyclase activity whereas others act via phospholipase C.

Members of the GPCR superfamily respond to a wide variety of ligands including small molecule amines (such as serotonin, dopamine, acetylcholine), lipid-derived mediators (such as LpA), amino acid derivatives (such as glutamate) and neurotransmitter peptides and hormones (such as neurokinin, galanin, glucagon, gastrin). Although GPCRs are activated by a broad range of ligands, it should be noted that individual GPCRs have a small and very specific repertoire of ligands. Based upon an analysis of the primary structure of a novel GPCR, it is now possible to classify them into specific sub-families, thereby narrowing the range of potential ligands.

In many cases, the endogenous ligands of GPCRs are relatively small, enabling them to be mimicked or blocked by synthetic analogues. For example drugs such as prazosin, doxazosin, cimetidine, ranitidine are all effective antagonists of their respective target GPCRs.

Thus, as the activation or inhibition of GPCRs can have therapeutic consequences, there is a continued need to provide new GPCRs and their associated agonists and antagonists.

Summary of the invention

According to one aspect of the present invention, there is provided an isolated polynucleotide comprising:

(a) a polynucleotide encoding the polypeptide as set forth in Figure 2;

(b) a polynucleotide encoding the polypeptide expressed by the DNA contained in National Collection of Industrial and Marine Bacteria Limited (NCIMB) Deposit No. _____;

(c) a polynucleotide comprising a nucleotide sequence of Figure 1;

(d) a polynucleotide comprising a nucleotide sequence that has at least 70-75% identity to the polynucleotide of any one of (a) to (c);

(e) a polynucleotide comprising a nucleotide sequence which is capable of hybridising to the polynucleotide of any one of (a) to (d); or

(f) a polynucleotide fragment of the polynucleotide of any one of (a) to (e).

Preferably, the polynucleotide comprises a nucleotide sequence that has at least 75-80% identity to the polynucleotide of any one of (a) to (c) above. More preferably, the polynucleotide comprises a nucleotide sequence that has at least 80-85% identity to the polynucleotide of any one of (a) to (c) above. Even more preferably, the polynucleotide comprises a nucleotide sequence that has at least 85-90% identity to the polynucleotide of any one of (a) to (c) above. Yet more preferably, the polynucleotide comprises a nucleotide sequence that has at least 90-95% identity to the polynucleotide of any one of (a) to (c) above. Most preferably, the polynucleotide comprises a nucleotide sequence that has greater than 95% identity to the polynucleotide of any one of (a) to (c) above.

Preferably, the polynucleotide encodes a mature polypeptide encoded by the DNA contained in NCIMB Deposit No. _____.

The polynucleotide described above preferably encodes a G-protein coupled receptor (GPCR).

The present invention also provides a polynucleotide probe or primer comprising at least 15 contiguous nucleotides of the polynucleotide described above.

The present invention yet further provides a vector comprising the polynucleotide described above.

According to a further aspect of the present invention, there is provided a host cell transformed or transfected with the vector described above. Preferably, the host cell is a mammalian, bacterial or yeast cell.

According to yet a further aspect of the present invention, there is provided a process for producing a polypeptide or fragment thereof comprising culturing said host cell under conditions sufficient for the expression of said polypeptide or fragment. Preferably, said polypeptide or fragment is expressed at the surface of said cell. The process preferably further includes recovering the polypeptide or fragment from the culture.

There is also provided by the present invention a process for producing cells capable of expressing a polypeptide or fragment thereof comprising transforming or transfecting cells with the vector described above.

According to a further embodiment of the present invention, there are provided cells produced by the process described above. There is also provided a membrane preparation of said cells.

According to another aspect of the present invention, there is provided a polypeptide comprising:

(a) a polypeptide having the deduced amino acid sequence translated from the polynucleotide sequence in Figure 1 and variants, fragments, homologues, analogues and derivatives thereof;

(b) a polypeptide of Figure 2 and variants, fragments, homologues, analogues and derivatives thereof; or

(c) a polypeptide encoded by the cDNA of NCIMB Deposit No. _____ and variants, fragments, homologues, analogues and derivatives of said polypeptide.

There is also provided by the present invention an antibody against the polypeptide described above.

The present invention yet further provides a compound which activates the polypeptide described above (an agonist) or which inhibits activation of the polypeptide described above (an antagonist).

According to another aspect of the present invention, there is provided a method for identifying a compound which binds to and activates the polypeptide described above comprising:

(a) contacting a compound with cells expressing on the surface thereof the polypeptide or a membrane preparation of said cells, said polypeptide being associated with a second component capable of providing a detectable signal in response to the binding of a compound to said polypeptide; said contacting being under conditions sufficient to permit binding of compounds to the polypeptide; and

(b) identifying a compound capable of polypeptide binding by detecting the signal produced by said second component.

According to another aspect of the present invention, there is provided a method for identifying a compound which binds to and inhibits activation of the polypeptide described above comprising:

(a) contacting (i) a detectable first component known to bind to and activate the polypeptide and (ii) a compound with cells expressing on the surface thereof the polypeptide or a membrane preparation of said cells, said polypeptide being associated with a second component capable of providing a detectable signal in response to the binding of a compound to said polypeptide; said contacting being under conditions sufficient to permit binding of compounds to the polypeptide; and

(b) determining whether the first component binds to the polypeptide by detecting the absence or otherwise of a signal generated from the interaction of the first component with the polypeptide.

As GPCRs are involved in signal transduction, agonists or antagonists of the polypeptide of the present invention can find use in interfering in the signal transduction process. Consequently, the present invention provides a compound which activates the polypeptide described above (an agonist) or which inhibits activation of the polypeptide described above (an antagonist) for use as a pharmaceutical. Such compounds, which can act as agonists or antagonists of the polypeptide, can therefore find use in the therapeutic areas which concern aspects of signal transduction. Therapeutically usefully areas include, but are not limited to, neurological disease, psychotherapeutics, urogenital disease, reproduction and sexual medicine, inflammation, cancer, tissue repair, dermatology, skin pigmentation, photoageing, frailty, osteoporosis, metabolic disease, cardiovascular disease, gastrointestinal disease, antiinfection, allergy and respiratory disease, sensory organ disorders, sleep disorders and hairloss.

Accordingly, there is also provided the use of the above compound (agonist) in the manufacture of a medicament in the treatment of a patient having need to activate a receptor.

There is also provided the use of the above compound (antagonist) in the manufacture of a medicament in the treatment of a patient having need to inhibit a receptor.

According to yet a further aspect of the invention, there is provided a method for the treatment of a patient having need to activate a receptor comprising administering to the patient a therapeutically effective amount of the above-described compound (agonist). Preferably, said compound (agonist) is a polypeptide and a therapeutically effective amount of the compound is administered by providing to the patient DNA encoding said compound and expressing said compound *in vivo*.

According to yet a further aspect of the invention, there is also provided a method for the treatment of a patient having need to inhibit a receptor comprising administering to the patient a therapeutically effective amount of the above-described compound (antagonist). Preferably, said

compound (antagonist) is a polypeptide and a therapeutically effective amount of the compound is administered by providing to the patient DNA encoding said compound and expressing said compound *in vivo*.

There is also provided by the present invention a method for the treatment of a patient having need to activate or inhibit a receptor, comprising administering to the patient a therapeutically effective amount of the antibody described above.

Yet further provided by the present invention is use of the antibody described above in the manufacture of a medicament for the treatment of a patient having need to activate or inhibit a receptor.

According to a further aspect of the present invention, there is provided a method of treatment of a patient having need to upregulate a receptor, comprising administering to the patient a therapeutically effective amount of the polypeptide of the present invention. Preferably, said therapeutically effective amount of the polypeptide is administered by providing to the patient DNA encoding said polypeptide and expressing said polypeptide *in vivo*.

There is also provided by the present invention, use of the polypeptide in the manufacture of a medicament for the treatment of a patient having need to upregulate a receptor.

According to yet a further aspect of the present invention, there are provided cells or an animal genetically engineered to overexpress, underexpress or to exhibit targeted deletion of the polypeptide of the present invention.

Detailed description of the invention

The present invention will now be described, by way of example only, with reference to the accompanying figures, wherein:

Figure 1 shows the nucleotide sequence coding for PFI-002. The ATG translation initiation codon is indicated by the first three letters. The stop codon is indicated by the last three letters.

Figure 2 shows the corresponding amino acid sequence coding for PFI-002.

Figure 3 shows a ClustalW Alignment of PFI-002 with SW|P20789|NTR1_RAT NEUROTENSIN RECEPTOR TYPE 1 (NT-R-1).

The polynucleotide which encodes the GPCR of the present invention was identified electronically and analysed using various bioinformatic tools. The GPCR encoded by the sequences described herein has been termed PFI-002.

The term "nucleotide sequence" as used herein refers to an oligonucleotide sequence or polynucleotide sequence, and variants, homologues, fragments and derivatives thereof (such as portions thereof). The nucleotide sequence may be DNA or RNA of genomic or synthetic or recombinant origin which may be double-stranded or single-stranded whether representing the sense or antisense strand.

Preferably, the term "nucleotide sequence" means DNA.

More preferably, the term "nucleotide sequence" means DNA prepared by use of recombinant DNA techniques (i.e. recombinant DNA).

In a preferred embodiment, the present invention does not cover the native nucleotide coding sequence according to the present invention in its natural environment when it is under the control of its native promoter which is also in its natural environment. For ease of reference, we shall call this preferred embodiment the "non-native nucleotide sequence".

As used herein "amino acid sequence" refers to peptide or protein sequences or portions thereof.

In a preferred embodiment, the present invention does not cover the native PFI-002 according to the present invention when it is in its natural environment and when it has been expressed by its native

nucleotide coding sequence which is also in its natural environment and when that nucleotide sequence is under the control of its native promoter which is also in its natural environment. For ease of reference, we shall call this preferred embodiment the "non-native amino acid sequence".

As used herein "naturally occurring" refers to a PFI-002 with an amino acid sequence found in nature.

As used herein "biologically active" refers to a PFI-002 having structural, regulatory or biochemical functions of the naturally occurring PFI-002.

As used herein, "immunological activity" is defined as the capability of the natural, recombinant or synthetic PFI-002 or any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.

The term "derivative" as used herein includes chemical modification of a PFI-002.

As used herein, the terms "isolated" and "purified" refer to molecules, either nucleic or amino acid sequences, that are removed from their natural environment and isolated or separated from at least one other component with which they are naturally associated.

The terms "variant", "homologue" or "fragment" in relation to the amino acid sequence for the preferred polypeptide of the present invention include any substitution of, variation of, modification of, replacement of, deletion of or addition of one (or more) amino acid from or to the sequence providing the resultant polypeptide has PFI-002 activity. In particular, the term "homologue" covers homology with respect to structure and/or function.

The terms "variant", "homologue" or "fragment" in relation to the nucleotide sequence coding for the preferred polypeptide of the present invention include any substitution of, variation of, modification of, replacement of, deletion of or addition of one (or more) nucleic acid from or to the sequence providing the resultant nucleotide sequence codes for or is capable of coding for a polypeptide having PFI-002 activity. In particular, the term "homologue" covers homology with respect to structure and/or function providing the resultant nucleotide sequence codes for or is

capable of coding for an enzyme having PFI-002 activity. With respect to sequence homology (i.e. identity), preferably there is at least 70-75%, more preferably at least 75-80%, more preferably at least 80-85%, more preferably 85-90%, yet more preferably 90-95%, and most preferably greater than 95% identity to the polynucleotide sequence shown in Figure 1.

In particular, the term "homology" as used herein may be equated with the term "identity". Relative sequence homology (i.e. sequence identity) can be determined by commercially available computer programs that can calculate % homology between two or more sequences. A typical example of such a computer program is CLUSTAL.

As used herein, the terms "variant", "homologue", "fragment" and "derivative" are synonymous with allelic variations of the sequences.

The term "variant" also encompasses sequences that are complementary to sequences that are capable of hydridising to the nucleotide sequences presented herein. Preferably, the term "variant" encompasses sequences that are complementary to sequences that are capable of hydridising under stringent conditions (e.g. 65°C and 0.1xSSC {1xSSC = 0.15 M NaCl, 0.015 Na3 citrate pH 7.0}) to the nucleotide sequences presented herein.

The present invention also covers nucleotide sequences that can hybridise to the nucleotide sequences of the present invention (including complementary sequences of those presented herein). In a preferred aspect, the present invention covers nucleotide sequences that can hybridise to the nucleotide sequence of the present invention under stringent conditions (e.g. 65°C and 0.1xSSC).

The term "vector" includes expression vectors and transformation vectors.

The term "expression vector" means a construct capable of *in vivo* or *in vitro* expression.

The term "transformation vector" means a construct capable of being transferred from one species to another.

The identification of PFI-002

PFI-002 was identified in unannotated genomic sequence information which is being released by the Genome Sequencing Centers by searching the sequences with known members of the G-protein coupled receptor (GPCR) family using the BLAST algorithm. In order to confirm that PFI-002 was a member of the GPCR family, a number of bioinformatics approaches were performed.

(a) BLAST Search against Swissprot

PFI-002 was searched against Swissprot using the BLAST algorithm (Basic Local Alignment Search Tool (Altshul SF (1993) J.Mol. Evol. 36:290-300; Altshul, SF et al (1990) J. Mol. Biol. 215:403-410)) to identify the closest protein match. In this case the top hit was to:

SW|P20789|NTR1_RAT NEUROTENSIN RECEPTOR TYPE 1 (NT-R-1) (HIGH-A....

These results indicate that PFI-002 is a member of the GPCR family.

(b) ClustalW Alignment of PFI-002 with SW|P20789|NTR1_RAT NEUROTENSIN RECEPTOR TYPE 1 (NT-R-1)

These results are shown in Figure 3.

(c) BLAST search against a non-redundant human GPCR database

PFI-002 was searched against a non-redundant human GPCR database comprising mainly sequences from Genbank and Geneseq Patents databases in order to identify the class of agonist for this receptor. The top ten hits are shown below:

O43664 GPCR2 : e-value = 6e-74, %Identity = 56%

AF034632 GP38 : e-value = 1e-31, %Identity = 37%

P30989 NTR1 : e-value = 2e-30, %Identity = 35%

U60179 GHSR : e-value = 3e-25, %Identity = 32%

Y10148 NTR2. : e-value = 4e-24, %Identity = 31%

P16473 TRFR : e-value = 4e-23, %Identity = 33%

P30874 SSR2 : e-value = 4e-22, %Identity = 31%

P35372 OPRM : e-value = 7e-22, %Identity = 31%

P30556 AT1B : e-value = 6e-21, %Identity = 31%

L08893 BRS3 : e-value = 8e-21, %Identity = 26%.

(e value = statistical likelihood of the hit occurring by chance)

These results demonstrate that PFI-002 is most closely similar to neurotensin receptors and they suggest that PFI-002 encodes a novel GPCR whose ligand is likely to be a peptide.

It will be appreciated that the foregoing is provided by way of example only and modification of detail may be made without departing from the scope of the invention.

Claims

1. An isolated polynucleotide comprising:

(a) a polynucleotide encoding the polypeptide as set forth in Figure 2;

(b) a polynucleotide encoding the polypeptide expressed by the DNA contained in National Collection of Industrial and Marine Bacteria Limited (NCIMB) Deposit No. _____;

(c) a polynucleotide comprising a nucleotide sequence of Figure 1;

(d) a polynucleotide comprising a nucleotide sequence that has at least 70-75% identity to the polynucleotide of any one of (a) to (c);

(e) a polynucleotide comprising a nucleotide sequence which is capable of hybridising to the polynucleotide of any one of (a) to (d); or

(f) a polynucleotide fragment of the polynucleotide of any one of (a) to (e).

2. The polynucleotide of claim 1, comprising a nucleotide sequence that has at least 75-80% identity to the polynucleotide of any one of (a) to (c).

3. The polynucleotide of claim 1, comprising a nucleotide sequence that has at least 80-85% identity to the polynucleotide of any one of (a) to (c).

4. The polynucleotide of claim 1, comprising a nucleotide sequence that has at least 85-90% identity to the polynucleotide of any one of (a) to (c).

5. The polynucleotide of claim 1, comprising a nucleotide sequence that has at least 90-95% identity to the polynucleotide of any one of (a) to (c).

6. The polynucleotide of claim 1, comprising a nucleotide sequence that has greater than 95% identity to the polynucleotide of any one of (a) to (c).

7. The polynucleotide of claim 1, wherein said polynucleotide encodes a mature polypeptide encoded by the DNA contained in NCIMB Deposit No. _____.

8. The polynucleotide of any one of the preceding claims which encodes a G-protein coupled receptor (GPCR).

9. A polynucleotide probe or primer comprising at least 15 contiguous nucleotides of the polynucleotide of any one of the preceding claims.

10. A vector comprising the polynucleotide of any one of the preceding claims.

11. A host cell transformed or transfected with the vector of claim 10.

12. The host cell of claim 11 which is a mammalian, bacterial or yeast cell.

13. A process for producing a polypeptide or fragment thereof comprising culturing the host cell of claim 11 or claim 12 under conditions sufficient for the expression of said polypeptide or fragment.

14. The process of claim 13, wherein said polypeptide or fragment is expressed at the surface of said cell.

15. The process of claim 13 or claim 14 which further includes recovering the polypeptide or fragment from the culture.

16. A process for producing cells capable of expressing a polypeptide or fragment thereof comprising transforming or transfecting cells with the vector of claim 10.

17. Cells produced by the process of claim 14.

18. A membrane preparation of the cells of claim 17.

19. A polypeptide comprising:

(a) a polypeptide having the deduced amino acid sequence translated from the polynucleotide sequence in Figure 1 and variants, fragments, homologues, analogues and derivatives thereof;

(b) a polypeptide of Figure 2 and variants, fragments, homologues, analogues and derivatives thereof; or

(c) a polypeptide encoded by the cDNA of NCIMB Deposit No. _____ and variants, fragments, homologues, analogues and derivatives of said polypeptide.

20. An antibody against the polypeptide of claim 19.

21. A compound (agonist) which activates the polypeptide of claim 19.

22. A compound (antagonist) which inhibits activation of the polypeptide of claim 19.

23. A method for identifying a compound which binds to and activates the polypeptide of claim 19 comprising:

(a) contacting a compound with cells expressing on the surface thereof the polypeptide of claim 19 or a membrane preparation of said cells, said polypeptide being associated with a second component capable of providing a detectable signal in response to the binding of a compound to said polypeptide; said contacting being under conditions sufficient to permit binding of compounds to the polypeptide; and

(b) identifying a compound capable of polypeptide binding by detecting the signal produced by said second component.

24. A method for identifying a compound which binds to and inhibits activation of the polypeptide of claim 19 comprising:

(a) contacting (i) a detectable first component known to bind to and activate the polypeptide of claim 19 and (ii) a compound with cells expressing on the surface thereof the polypeptide of claim

19, or a membrane preparation of said cells, said polypeptide being associated with a second component capable of providing a detectable signal in response to the binding of a compound to said polypeptide; said contacting being under conditions sufficient to permit binding of compounds to the polypeptide; and

(b) determining whether the first component binds to the polypeptide by detecting the absence or otherwise of a signal generated from the interaction of the first component with the polypeptide.

25. The compound of claim 21 or claim 22 for use as a pharmaceutical.

26. Use of the compound (agonist) of claim 21 in the manufacture of a medicament in the treatment of a patient having need to activate a receptor.

27. Use of the compound (antagonist) of claim 22 in the manufacture of a medicament in the treatment of a patient having need to inhibit a receptor.

28. A method for the treatment of a patient having need to activate a receptor comprising administering to the patient a therapeutically effective amount of the compound of claim 21.

29. The method of claim 28, wherein said compound is a polypeptide and a therapeutically effective amount of the compound is administered by providing to the patient DNA encoding said compound and expressing said compound *in vivo*.

30. A method for the treatment of a patient having need to inhibit a receptor comprising administering to the patient a therapeutically effective amount of the compound of claim 22.

31. The method of claim 30, wherein said compound is a polypeptide and a therapeutically effective amount of the compound is administered by providing to the patient DNA encoding said compound and expressing said compound *in vivo*.

32. A method for the treatment of a patient having need to activate or inhibit a receptor, comprising administering to the patient a therapeutically effective amount of the antibody of claim 20.

33. Use of the antibody of claim 20 in the manufacture of a medicament for the treatment of a patient having need to activate or inhibit a receptor.

34. A method of treatment of a patient having need to upregulate a receptor, comprising administering to the patient a therapeutically effective amount of the polypeptide of claim 19.

35. The method of claim 34, wherein said therapeutically effective amount of the polypeptide is administered by providing to the patient DNA encoding said polypeptide and expressing said polypeptide *in vivo*.

36. Use of the polypeptide of claim 19 in the manufacture of a medicament for the treatment of a patient having need to upregulate a receptor.

37. Cells or animal genetically engineered to overexpress the polypeptide of claim 19.

38. Cells or animal genetically engineered to underexpress the polypeptide of claim 19.

39. Cells or animal genetically engineered to exhibit targeted deletion of the polypeptide of claim 19.

Abstract

NOVEL POLYPEPTIDE

Polynucleotide and polypeptide sequences are described. The polypeptide sequences comprise: (a) a polypeptide having the deduced amino acid sequence translated from the polynucleotide sequence in Figure 1 and variants, fragments, homologues, analogues and derivatives thereof; (b) a polypeptide of Figure 2 and variants, fragments, homologues, analogues and derivatives thereof; or (c) a polypeptide encoded by the cDNA of NCIMB Deposit No. _____ and variants, fragments, homologues, analogues and derivatives of said polypeptide.

Figure 1

Nucleotide sequence coding for PFI-002

ATGGAAAAACTTCAGAATGCTTCCTGGATCTACCAGCAGAAACTAGAAGATCCATTCC
AGAAACACCTGAACAGCACCGAGGAGTATCTGGCCTTCCTCTGCGGACCTCGGCGCAG
CCACTTCTTCCTCCCCGTGTCTGTGGTGTATGTGCCAATTTTTGTGGTGGGGGTCATTGG
CAATGTCCTGGTGTGCCTGGTGATTCTGCAGCACCAGGCTATGAAGACGCCCACCAAC
TACTACCTCTTCAGCCTGGCGGTCTCTGACCTCCTGGTCCTGCTCCTTGGAATGCCCCT
GGAGGTCTATGAGATGTGGCGCAACTACCCTTTCTTGTTCGGGCCCGTGGGCTGCTACT
TCAAGACGGCCCTCTTTGAGACCGTGTGCTTCGCCTCCATCCTCAGCATCACCACCGTC
AGCGTGGAGCGCTACGTGGCCATCCTACACCCGTTCCGCGCCAAACTGCAGAGCACCC
GGCGCCGGGCCCTCAGGATCCTCGGCATCGTCTGGGGCTTCTCCGTGCTCTTCTCCCTG
CCCAACACCAGCATCCATGGCATCAAGTTCCACTACTTCCCCAATGGGTCCCTGGTCCC
AGGTTCGGCCACCTGTACGGTCATCAAGCCCATGTGGATCTACAATTTCATCATCCAGG
TCACCTCCTTCCTATTCTACCTCCTCCCCATGACTGTCATCAGTGTCCTCTACTACCTCA
TGGCACTCAGAGTGAGTATCTAG

Figure 2

Amino acid sequence coding for PFI-002

MEKLQNASWIYQQKLEDPFQKHLNSTEEYLAFLCGPRRSHFFLPVSVVYVPIFVVGVIGNV
LVCLVILQHQAMKTPTNYYLFSLAVSDLLVLLLGMPLEVYEMWRNYPFLFGPVGCYFKTA
LFETVCFASILSITTVSVERYVAILHPFRAKLQSTRRRALRILGIVWGFSVLFSLPNTSIHGIKF
HYFPNGSLVPGSATCTVIKPMWIYNFIIQVTSFLFYLLPMTVISVLYYLMALRVSI

Figure 3

ClustalW Alignment of PFI-002 with SW|P20789|NTR1_RAT NEUROTENSIN RECEPTOR TYPE 1 (NT-R-1) (HIGH-A...

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CLUSTAL W (1.74) multiple sequence alignment

NTR1_RAT        MHLNSSVPQGTPGEPDAQPFSGPQSEMEATFLALSLSNGSGNTSESDTAGPNSDLDVNTD
PFI-002         ------------MEKLQNASWIYQQKLEDPFQKH------LNSTEEYLAFLCGPRRS---
                             *   :.    *.::* .*          *::*.  *    .

NTR1_RAT        IYSKVLVTAIYLALFVVGTVGNSVTAFTLARKKSLQSLQSTVHYHLGSLALSDLLILLLA
PFI-002         HF-FLPVSVVYVPIFVVGVIGNVLVCLVILQ---HQAMKTPTNYYLFSLAVSDLLVLLLG
                 :  : *:.:*:.:****.:** :..:.: :    *::::..:*:* ***:****:***.

NTR1_RAT        MPVELYNFIWVHHPWAFGDAGCRGYYFLRDACTYATALNVASLSVERYLAICHPFKAKTL
PFI-002         MPLEVY-EMWRNYPFLFGPVGCYFKTALFETVCFASILSITTVSVERYVAILHPFRAKLQ
                **:*:*  :* ::*: ** .**     * ::  :*: *.::::*****:** ***:**

NTR1_RAT        MSRSRTKKFISAIWLASALLAIPMLFTMGLQN-RSGDG-THPGGLVCTPIVDTATVKVVI
PFI-002         STRRRALRILGIVWGFSVLFSLPNTSIHGIKFHYFPNGSLVPGSATCTVIKPMWIYNFII
                 :* *: :::. :*  *.*:::*     *::     :*   **. .** *      :.:*

NTR1_RAT        QVNTFMSFLFPMLVISILNTVIANKLTVMVHQAAEQGRVCTVGTHNGLEHSTFNMTIEPG
PFI-002         QVTSFLFYLLPMTVISVLYYLMALR-----------------------------------
                **.:*: :*:** ***:*  ::* :

NTR1_RAT        RVQALRHGVLVLRAVVIAFVVCWLPYHVRRLMFCYISDEQWTTFLFDFYHYFYMLTNALF
PFI-002         ------------------------------------------------------------

NTR1_RAT        YVSSAINPILYNLVSANFRQVFLSTLACLCPGWRHRRKKRPTFSRKPNSMSSNHAFSTSA
PFI-002         ------------------------------------------------------------

NTR1_RAT        TRETLY
PFI-002         ------
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